II. RESPONSE TO OFFICE ACTION

A. Status of the Claims

Claims 1-89 were pending prior to the Office Action dated November 17, 2005 ("Action"). Claims 1-38 and 48-62 were withdrawn from consideration. Claims 39-47 and 63-89 were rejected in the Action.

Claims 39 and 68 are amended in this response to clarify the claims based on the language in the specification. This amendment does not affect the basis of any rejection of the claims. Support for this amendment can be found at least at page 69, lines 16-20, which indicates that sequences may have a certain percentage of "amino acids that are identical or functionally equivalent to the amino acids of SEQ ID NO:2. . . ." Therefore, no new matter has been added.

B. The Claims Are Adequately Described

The Action rejects claims 39-47 and 63-89 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. While it admits that seven specific polypeptides are disclosed in the specification, including SEQ ID NO:2 (Action at page 11-12), it asserts that the claims encompass variants of SEQ ID NO:2 which are different from the sequence disclosed in SEQ ID NO:2, and these variants have not been adequately described. Action at page 3. The Action further argues that the specification describes only one species of what it characterizes as a vast genus because it provides only SEQ ID NO:2 (the Action also concedes that seven polypeptides are disclosed). It also contends that the specification does not disclose any other variants of Fortilin that maintain activity, nor does the specification indicate which amino acid of Fortilin can be changed or deleted and result in a "biologically active" Fortilin variant. The Action also alleges that there is no structure function relationship described such that one of skill in the art could be able to clearly recognize any critical structural elements of Fortilin. Consequently, the Examiner asserts that the specification does not adequately

describe a sufficient number of "representative species" encompassed by the claims. Finally, the Action cites different references allegedly commenting on whether homology relates to function and it asserts that "the claimed genus of 'Fortilin' polypeptides has the potential of encompassing polypeptides that have "different function." Action at page 5. Applicants respectfully traverse this rejection.

1. The Specification Describes What Is Claimed by Chemical Structure

"The purpose of the written description requirement is to prevent an applicant from later asserting that he invented that which he did not; the applicant for a patent is therefore required 'to recount his invention in such detail that his future claims can be determined to be encompassed within his original creation.'" *Moba v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319 (Fed. Cir. 2003) (citing *Amgen Inc. v. Hoechst Marion Roussel Inc.*, 314 F.3d 1313, 1330 (Fed. Cir. 2003)). An accepted standard for the written description requirement is: "Although the applicant does not have to describe exactly the subject matter claimed, the description must clearly allow persons of ordinary skill in the art to recognize that he or she invented **what is claimed**." *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1562-1563 (Fed. Cir. 1991) (emphasis added). Written description is met if "the disclosure of the application relied upon reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Lampi*, 228 F.3d at 1378. Again, Applicants emphasize that for purposes of the written description inquiry, the invention is whatever is **actually claimed**. *Vas-Cath*, 935 F.2d at 1563-1564. An inventor is "in possession" of an invention if the patent uses "such descriptive means as words, structures, figures, diagrams, formulas, *etc.*, that fully set forth the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed. Cir. 1997). Furthermore, an application must be presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption. MPEP 2163.04 (citing

In re Marzocchi, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971)). "The examiner must, therefore, have a reasonable basis to challenge the inadequacy of the written description. The examiner has the initial burden of presenting by a preponderance of the evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims." *Id.* (citing *In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976). As is discussed in further detail below, the Examiner has not fulfilled this burden because he relies upon an argument of function and structure, yet there is no explanation of how this is relevant to the claimed invention.

The Action acknowledges that the specification does provide adequate written description of a human fortilin polypeptide and SEQ ID NO:2 (Action at page 3 and page 4). Each of the rejected claims sets forth methods involving a "Fortilin polypeptide with at least 70% of its amino acids identical or functionally equivalent to SEQ ID NO:2 or that has at least 20 contiguous amino acids from SEQ ID NO:2." The Federal Circuit has stated:

> the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or **partial structure**, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of characteristics.'

Enzo Biochem., Inc. v. Gen-Probe Inc., 296 F.3d 1316, 1324, 63 U.S.P.Q.2d 1609, 1613 (Fed. Cir. 2002) (original emphasis omitted, other emphasis added, alterations in original).

This much the specification provides. Appellants have disclosed the sequence of SEQ ID NO:2, which is 172 amino acids in length. As a result, Appellants have described hundreds and thousands of polypeptides that can be employed in these methods as the skilled artisan would know these sequences of polypeptides with at least 70% of its amino acids identical or functionally equivalent to SEQ ID NO:2 or that has at least 20 contiguous amino acids of SEQ ID NO:2. The Examiner has not explained how the structural requirements set forth in the

claims is insufficient to describe a substantial portion of the genus he asserts is covered by the claims. Based on the number of disclosed species, the specification necessarily satisfies the written description requirement because it reasonably conveys to one of skill in the art that they had possession of the claimed subject matter. *In re Daniels*, 144 F.3d 1452, 1456, 46 USPQ2d 1788, 1790.

2. A Representative Number of Species Is Provided

The number of species described simply by disclosing the 172 residues of SEQ ID NO:2 is enormous, and there should be no dispute that thousands of species within the scope of the claims are described in Applicants' specification because SEQ ID NO:12 is provided. "A specification may, within the meaning of 35 U.S.C. §112 para. 1, contain a written description of a broadly claimed invention without describing all species that claim encompasses." *Utter v. Hiraga*, 845 F.2d 993, 998 (Fed. Cir. 1988).

Moreover, to satisfy the written description requirement, "an applicant is not required to describe in the specification every conceivable and possible future embodiment of his invention." *Cordis*, 339 F.3d at 1365 (citing *Rexnord Corp. v. Laitram Corp.*, 274 F.3d 1336, 1344 (Fed. Cir. 2001)). The use of variants of the full-length sequence in the screening method of the invention represents simply other embodiments, none of which are required in order to achieve the utility of the invention.

In addition, the present scenario is distinguishable from cases like *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharm. Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991) because the present claims recite a specific structure (reference to SEQ ID NO:2) and are not characterized in terms of function only. Consequently, the Examiner has also not set forth *why* Appellants need to provide a reasonable number of representative species in the context of the claimed invention. There can be no dispute that Appellants have described

embodiments of the claimed invention pertaining to, for example, "polypeptides with at least 70% of its amino acids identical or functionally equivalent to SEQ ID NO:2 or that has at least 20 contiguous amino acids of SEQ ID NO:2" by providing SEQ ID NO:2.

Furthermore, the MPEP sets forth the legal basis for providing an adequate number of species to satisfy the written description requirement:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species. A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

MPEP §2163.05. The claimed invention covers processes involving a Fortilin polypeptide having a particular sequence (SEQ ID NO:2). Thus, Appellants have described a representative number of species that are representative of the entire genus because the variations of any Fortilin polypeptide are limited by the recited structural limitations. Moreover, because of the structural recitation in the claims, a sufficient number has been disclosed because a "person of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by members of the genus in view of the species disclosed." *See* Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112 ¶ 1, "Written Description" Requirement, FEDERAL REGISTER, Vol. 66, No. 4 1099, 1106 (January 4, 2001).

Therefore, given that thousands of species are disclosed in the disclosure of SEQ ID NO:2, the examiner has failed to show by a preponderance of evidence that the skilled person would not recognize that Appellants were in possession of the claimed invention. On this basis alone the rejection is improper and should be withdrawn.

3. Enablement Rejection Has Been Overcome

Applicants further note that the contentions raised in the Action sound more like an enablement rejection than a written description rejection. Several references have been cited as relevant to the issue of structure versus function. The Action cites Henikoff *et al.* for the proposition that one skilled in the art would not accept mere homology as establishing a function of protein because gene products may acquire new specificities, altered recognition properties, or modified functions. Action at page 11. It also cites Witkowski *et al.* and Seffernick *et al.* for the contention that the art recognizes that a high degree of structural homology may not result in functional homology.

These statements in the rejection sound like the issue involves enablement, instead of written description, because they suggest the skilled artisan would not know which Fortilin polypeptides could be used in the context of the claimed invention. However, given that the claims specify by structure which molecules qualify as the polypeptide to be used in the claim, these arguments are not appropriate for assessing written description.

As further confirmation that the arguments are not related to written description, Applicants note that the cases of *Amgen* and *Fiers* that are cited by the Action are **enablement** cases as explained in MPEP §2164.08. There is no pending enablement rejection of the claims, as this has already been withdrawn in this action. Therefore, reliance on these cases in the context of a written description rejection demonstrates how the law has been misapplied and that this rejection is not a proper written description rejection.

Additionally, even <u>if</u> those cases were to considered somehow to apply to the present case, the facts here differ from the facts of those cases. Significantly, this is not a situation as in *Amgen* or *Fiddes* in which the <u>claims</u> set forth only the name of a gene or polypeptide and

provides no structural information. As repeated throughout this response, the present claims describe the relevant polypeptide by reciting structural (sequence) requirements.

4. Biologically Active Variants of Fortilin Are Not Required by Claim

As discussed in the previous section, the Action cites a number of references and argues that these references show the claims cover a genus of Fortilin polypeptides that potentially encompasses polypeptides having different function. However, this is not relevant to the written description inquiry because the claims set forth that the Fortilin polypeptide contains with at least 70% of its amino acids identical or functionally equivalent to SEQ ID NO:2 or that it has at least 20 contiguous amino acids of SEQ ID NO:2. There is no requirement in the claims that Fortilin polypeptides are "biologically active" or that they have a certain function. As mentioned above, the written description requirement applies to *what is claimed.*

Applicants remind the Examiner that the claims are directed to identifying modulators of Fortilin, and as such, could conceivably cover antibodies that specifically recognize Fortilin. These antibodies could be identified and characterized using the Fortilin polypeptides set forth in the claims—a "Fortilin polypeptide with at least 70% of its amino acids identical or functionally equivalent to SEQ ID NO:2 or that has at least 20 contiguous amino acids of SEQ ID NO:2"—and the issue of function or biological activity need not be an issue in the context of the independent claim. It is not clear how these different references show that the inventors were not in possession of methods involving the recited Fortilin polypeptides.

5. Similar Rejection Overturned by Board

Applicants submit a copy of a Board decision involving a written description rejection and claims similar to those here (Exhibit 1). While this case is neither written for publication or binding precedent, and Applicants acknowledge that each case is decided on its own merits, nonetheless the decision by the Board is illustrative. In *Ex Parte Friedberg* the Board states:

> In this case, the complete structure of SEQ ID NO:2 and SEQ ID NO:4 [polypeptide sequence for human and for another mammal]has been described, and the polypeptides of the claimed genus share at least 10 contiguous amino acids of the structure of SEQ ID NO:2 or SEQ ID NO:4. Thus, the structural features that are common to the genus make up at least 10 contiguous amino acids of the structure set forth in SEQ ID NO:2 or SEQ ID NO:4. The examiner has not adequately explained why this degree of structural similarity is inadequate to "constitute a substantial portion of the genus," as required by Lilly. Accordingly, we reverse the rejection of [the] claims under 35 U.S.C. § 112, first paragraph, [that the] specification fails to adequately describe the claimed invention.

Ex Parte Friedberg, at page 6. Similar to this case, the claims in *Friedberg* recited a polypeptide with a certain number of amino acids from the referenced sequence. The Board agreed with the Friedberg *et al.* applicants that the claims were adequately described in providing the referenced sequence. Applicants believe the Board's decision in *Friedberg* with respect to the written description requirement accurately reflects the current caselaw.

For the foregoing reasons, Applicants respectfully request the written description rejection be withdrawn.

C. No New Matter Has Been Added to Claim 68

The Action rejects claims 68 and 70-83 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement because the amendment to claim 68 allegedly introduced new matter into the application. More specifically, it contends that amending the claims to recite a "recombinant cell expressing the Fortilin polypeptide" is not supported by the specification because there is allegedly no "support for a method of identifying a modulator of Fortilin activity using a transfected cell wherein the cell expresses endogenous Fortilin. Applicants respectfully traverse this rejection on two grounds.

1. Examiner Is Looking for Written Description of a Single Embodiment

Rejected independent claim 68 recites a method involving "contacting a candidate modulator with a recombinant cell expressing a Fortilin polypeptide with at least 70% of its

amino acids identical or functionally equivalent to SEQ ID NO:2 or that has at least 20 contiguous amino acids from SEQ ID NO:2." The Examiner argues that this claim contains new matter because there is no disclosure of a "method of identifying a modulator of Fortilin activity using a transfected cell where in the cell expresses endogenous Fortilin." Action at page 10.

Applicants contend that this is not the proper standard for evaluating new matter because it identifies a single embodiment—that the cell expresses endogenous Fortilin—which is not specifically recited in the claims. This is inappropriate. The Patent Office routinely issues claims directed to a genus, as well as dependent claims directed to a species within that genus when the only disclosure in the application is of the genus and the recited species. For instance, Applicants can imagine an independent claim directed to a vector containing "a promoter" that directs expression of gene X and a dependent claim that states the promoter is promoter1, promoter2, or promoter3. It would be illegitimate for an examiner to reject the independent claim for not describing some random promoter4 simply because the dependent claim recited all the promoters disclosed in the application.

Even if this were an appropriate standard for evaluating new matter, the specification does support the use of endogenous Fortilin. It states: "Determination of which molecules are suitable modulators of Fortilin may be achieved using assays familiar to those of skill in the art—some of which are disclosed herein—and may include, for example, the use of **native** and/or recombinant Fortilin." (Emphasis added). Page 26, lines 18-20. This is confirmed by the Declaration of Dr. Rick Wetsel ("Wetsel Declaration") (Exhibit 2) at ¶ 8.

2. Specification Describes Things Other Than Exogenous Fortilin

As discussed above, even if the Action considers dependent claim 69 to be disclosed, the more appropriate perspective for evaluating whether there is new matter in independent claim 68

is whether the specification discloses a cell that is recombinant by virtue of it expressing *something other than exogenous Fortilin.* The Wetsel Declaration provides evidence that "had a person skilled in molecular biology, particularly with knowledge of assays involving recombinant DNA technology and protein function, read this specification in October of 2001, the specification as a whole would have readily described to them the invention described in claim 68." Wetsel Declaration ¶ 7. Dr. Wetsel states, "More specifically, the specification indicates that the invention includes screening methods involving recombinant cells that are considered recombinant because they contain exogenous sequences for a number of different nucleic acids, in addition to exogenous Fortilin." *Id.* The Wetsel Declaration sets forth a number of passages that support these statements (¶ 8):

- *Page 9, lines 1-18*: Specification indicates that screening methods are contemplated to be part of the present invention. It further explains that "this method includes contacting the Fortilin polypeptide with a candidate substance and assaying whether the candidate substance modulates the Fortilin polypeptide."
- *Page 26, lines 18-20*: In another part of the specification, it states, "Determination of which molecules are suitable modulators of Fortilin may be achieved using assays familiar to those of skill in the art—some of which are disclosed herein—and may include, for example, the use of **native** and/or recombinant Fortilin." (Emphasis added).
- *Page 65, line 12-105*: The first sentence in this section states that the "present invention concerns polynucleotides, isolatable from cells, that are free from total genomic DNA and that are capable of expressing all or part of a protein or polypeptide." (Page 65, lines 14-16). This section is directed to nucleic molecules, such as "Polynucleotides

Encoding Native Proteins or Modified Proteins" (page 65, lines 12-13). Significantly, there is a passage that states:

> In particular embodiments, the invention concerns isolated DNA segments and recombinant vectors incorporating DNA sequences that encode a wild-type, polymorphic, or mutant Fortilin or Fortilin modulator polypeptide or peptide that includes within its amino acid sequence a contiguous amino acid sequence in accordance with, or essentially corresponding to a native polypeptide. Thus, an isolated DNA segment or vector containing a DNA segment may encode, for example, a Fortilin modulator that can inhibit or reduce Fortilin activity.

(Page 67, lines 9-15). This passage makes it clear that a Fortilin modulator may be recombinant. Additionally, this section of the application also includes a discussion of vectors starting at page 72, which also describes various promoters such as "recombinant or heterologous promoter" (page 73, lines 26-29). Moreover, this section also includes a discussion of "host cells" in which it is stated that "a host cell may be 'transfected' or 'transformed, which refers to a process by which exogenous nucleic acid, such as a modified protein-encoding sequence, is transferred or introduced into a host cell." (Page 84, lines 20-30). Such a host cell would be considered a "recombinant" cell.

- *Page 106, line 19-page 110, line 29*: This section is entitled " Screening Methods Involving FORTILIN," and it describes how to identify a Fortilin modulator. It states, "one generally will determine the activity or level of inhibition of Fortilin in the presence and absence of the candidate substance, wherein a modulator is defined as any substance that alters these characteristics. For example, a method generally comprises: (a) providing a candidate modulator; (b) admixing the candidate modulator with an isolated compound or cell expressing the compound; (c) measuring one or more characteristics of the compound or cell in step (b); and (d) comparing the characteristic measured in step (c) with the characteristic of the compound or cell in the absence of said candidate

modulator, wherein a difference between the measured characteristics indicates that said candidate modulator is, indeed, a modulator of the compound or cell." (Page 106, line 27-page 107, line 11). It also states how "[a]ssays may be conducted in cell free systems, in isolated cells, or in organisms including transgenic animals." (Page 107, lines 13-14). The cells of such transgenic animals could be considered recombinant cells; moreover, this passage does not limit transgenic animals to those that express only an exogenous Fortilin polypeptide.

- *Page 159-160*: In Example 9, experiments are described involving a recombinant cell (cell transfected with two different plasmids) that expresses GAL4-DNA-BD (binding domain)-Fortilin and VP16-DNA-AD (activating domain)-p53. In addition to expressing exogenous Fortilin, these cells express other nucleic acids that are exogenous to the cells and thus, the cell can be considered "recombinant" by virtue of being transfected with other non-Fortilin nucleic acids sequences.

The Wetsel Declaration concludes, "These cited passages make it clear to me that the patent application describes what is recited in claim 68, in particular, the use of a recombinant cell expressing Fortilin polypeptide in a method of screening for Fortilin modulators. This includes cells that are recombinant because they express exogenous nucleic acids other than exogenous Fortilin. Moreover, the specification makes clear that the cell may express native Fortilin as well. *See* page 26, lines 18-20." *Id.* at ¶ 9.

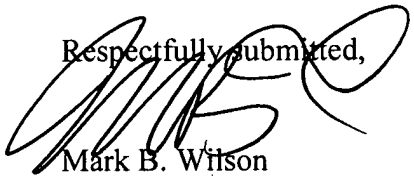
Applicants contend that no new matter has been added to the application and they respectfully request this rejection be withdrawn.

CONCLUSION

Applicants believe that the foregoing remarks fully respond to all outstanding matters for this application. Applicants respectfully request that the rejections of all claims be withdrawn so they may pass to issuance.

Should the Examiner desire to sustain any of the rejections discussed in relation to this Response, the courtesy of a telephonic conference between the Examiner, the Examiner's supervisor, and the undersigned attorney at 512-536-3055 is respectfully requested.

Respectfully submitted,



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